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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,447	04/22/2005	Aldo Pinchera	B-0496 PUS	1713

31834 7590 11/02/2007

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EXAMINER	
RAE, CHARLESWORTH E	

ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
11/02/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/532,447	PINCHERA ET AL.	
	Examiner	Art Unit	
	Charleswort Rae	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-15 and 17-25* is/are pending in the application.

4a) Of the above claim(s) *17-24* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-15 and 25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *17-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's arguments/amendment, filed 2/27/07, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of actions being applied to the instant application.

Applicant's statement that the specification has been amended to correct the misspelling of the term "highlights" at page 4, line 19 is acknowledged and made of record.

The amendments to the specification, filed 2/27/07, are entered of record. However, it is requested that applicant submit a clean copy of said amendment, along with an accompanying statement on a different sheet stating that no new matter has been added by this amendment, as part of the next communication to the Office.

It is noted that new claims 17-24 are directed towards a different statutory class (i.e. method of treatment) than the previously presented claims (i.e. product claims). Thus, a restriction requirement is herein issued in view of applicant's constructive election of the invention to the product at original presentation for examination purposes.

Status of the Claims

Claims 9-15 and 17-25 are currently pending in this application and are the subject of the Office action.

Claims 1-8 and 16 are canceled; claims 9-15 are amended; and claims 17-25 are new.

Claims 17-24 are withdrawn for examination purposes for being directed towards non-elected subject matter as discusses herein.

Claims 9-15 and 25 are presented for examination.

Restriction

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

I. Claims 9-13, drawn to a pharmaceutical composition for oral administration.

II. Claims 14-15 and 25, drawn to a kit.

III. Claims 17-24, drawn to a method of treating a subject with a pathology due to organic deficiency of triiodothyronine.

The inventions represented above as Groups I-III relate to a general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they do not share the same or corresponding technical features. Specifically, the technical feature of Group I, is the pharmaceutical composition; the technical feature of Group II is a kit; and the technical feature of Group III is a method of

treating a subject with a pathology. Further, the inventions lack unity in view of Lopresti. Thus, the requirement is proper as the inventions represented above as Groups I-III lack unity of invention under PCT Rule 13.1.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder**. Further, note that the prohibition

against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues.

See MPEP § 804.01.

> Effective November 1, 2007, if applicant wishes to present more than 5 independent claims or more than 25 total claims in an application, applicant will be required to file an examination support document (ESD) in compliance with 37 CFR 1.265 before the first Office action on the merits (hereafter "5/25 claim threshold"). See Changes to Practice for Continued Examination Filings, Patent Applications Containing Patentably Indistinct Claims, and Examination of Claims in Patent Applications, 72 Fed. Reg. 46715 (Aug. 21, 2007), 1322 Off. Gaz. Pat. Office 76 (Sept. 11, 2007) (final rule). The changes to 37 CFR 1.75(b) apply to any pending applications in which a first Office action on the merits (FAOM) has not been mailed before November 1, 2007. Withdrawn claims will not be taken into account in determining whether an application exceeds the 5/25 claim threshold. For more information on the final rule, please see http://www.uspto.gov/web/offices/pac/dapp/opla/presentation/clmcontfinalrule.html.
>
> In response to the restriction requirement set forth in this Office action, applicant is required to file an election responsive to the restriction requirement. Applicant may not file a suggested restriction requirement (SRR) in lieu of an election responsive to the restriction requirement as a reply. A SRR alone will not be considered a *bona-fide* reply to this Office action.
>
> If applicant elects an invention that is drawn to no more than 5 independent claims and no more than 25 total claims, applicant will not be required to file an ESD in compliance with 37 CFR 1.265 that covers each of the elected claims. If the elected invention is drawn to more than 5 independent claims or more than 25 total claims, applicant may file an amendment canceling a number of elected claims so that the elected invention would be drawn to no more than 5 independent claims and no more than 25 total claims.
>
> If the restriction requirement is mailed on or after November 1, 2007, applicant is also required to file an ESD in compliance with 37 CFR 1.265 that covers each of the elected claims, unless the elected invention is drawn to no more than 5 independent claims and no more than 25 total claims taking into account any amendment to the claims. To avoid the abandonment of the application, the ESD (if required) and the election must be filed within **TWO MONTHS** from the mailing date of this Office

action. The two-month time period for reply is extendable under 37 CFR 1.136.

If the restriction requirement is mailed before November 1, 2007, the election must be filed within **ONE MONTH** or THIRTY DAYS, whichever is longer, from the mailing date of this Office action. The time period for reply is extendable under 37 CFR 1.136. Furthermore, if the elected invention is drawn to more than 5 independent claims or more than 25 total claims taking into account any amendment to the claims, the Office will notify applicant and provide a time period in which applicant is required to file an ESD in compliance with 37 CFR 1.265 covering each of the elected claims or amend the application to contain no more than 5 independent elected claims and no more than 25 total elected claims.

Response to applicant's arguments/remarks

Objection to the specification

The objection is withdrawn in view of applicant's amendment to the specification to correct the misspelling of the term "unexpectedly."

Rejections under 112, second para (claims 3, 5, 9, 15-16)

Applicant assert that this rejection has been rendered moot by the amendment to the claims.

In response, the rejection is withdrawn with respect to claims 3, 5, 15 and 16 as applicant's argument is found to be persuasive.

The rejection is being maintained with respect to instant claim 9 for the following reason:

a) Claim 9 recites the term "such as." Similar to the term "like," the term "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP 2173.05(d). It is suggested that this rejection may be overcome by deleting the term "such as"

and replacing it with the term "selected from the group consisting of excipients, diluents, dissolvents, solvents, carriers, dyestuffs, flavourings and sweeteners" provided the amendment is supported by the specification as originally filed.

Rejection under 102(b) (claims 1-7, 9 and 16)

This rejection is withdrawn.

Rejection under 103(a) (claims 8 and 10-15)

This rejection is withdrawn.

REJECTIONS

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 9-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 9, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Dependent claim 10-13 are rejected for the same reasons as these claims fail to correct the deficiency of the claim 9 from which they depend either directly or indirectly.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-15 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lopresti et al. ("Characteristics of 3,5,3'-Triiodothyronine Sulfate Metabolism in Euthyroid Man", Journal of Clinical Endocrinology and Metabolism, Vol. 73, No. 4, 1992, pages 703-709, item "CA" on PTO 1449 filed on 02/14/2006; already made of record, in view of Mol et al., in view of Herfindal et al. (Herfindal et al. In: Clinical Pharmacy and Therapeutics. 1992, pages 289-291), and in further view of Fisher et al. (US Patent 4254095).

Lopesti et al. teach that two subjects were given T3S orally in an amount of 25 μCi mixed in 20 ml 1% human albumin solution in distilled water (page 704, col. 1, 4th para); Lopresti et al. disclose that 25 μCi of 3,5,3'-Triiodothyronine Sulfate (T_3S) in a 5% human albumin solution was administered to human volunteers (page 704, left column, last paragraph). The term *"triiodothyronine sulfate at a dose ranging from 5 to 1000 μg"* as recited in claim 9 is reasonably construed to be equivalent to *"triiodothyronine sulfate at a dose ranging from 5 to 1000 μCi"* in view of Fisher et al. (US Patent 4254095. Fisher et al. teach that 1 *μCi = 1 microgram* (see reference claim 18). Based on the teaching of Fisher et al., it necessarily follows that the oral dose of T3S (i.e. 25 micrograms) taught by Lopresti et al. overlaps with the instant claimed dose range of T3S (i.e. 5 to 1000 micorgrams). Claim 9 recites the term "[a pharmaceutical composition comprising the compound triiodothyronine sulfate (T_3S). " Claim 9 also recites the term "oral administration," and the term "additives such as excipients, diluents, dissolvents, solvents, carriers, ..." which overlaps with the teaching of Lopresti et al. .i.e. water and albumin as taught by Lopresti may be reasonably construed to be additives excipients/diluents/ solvents/carriers. Lopresti et al. also teach a method for estimating oral absorption an in vivo biological activity of T3S and T4 (page 704, col. 1, second para.). In view of the teaching of Lopresti et al., the dosage amounts of T3S recited in claims 9, 10, 11. 12, 13, 15, and 25 are reasonably construed to be dose optimization and within the skill and scope of knowledge an artisan skilled in the art. The term "a pharmaceutical composition for oral use comprising an

effective amount of thyroxine" as recited in claim 14, is similarly construed to be be within the skill and knowledge of an artisan skilled in the art in view of the teaching of Lopresti et al. Claims 14, 15 and 25 recite the term a "kit."The teaching of Lopresti et al. and Herfindal et al. differ from the claimed invention in that claims 14, 15 and 25 recite a kit. Judicial notice is taken that the packaging and labeling instructing use of a composition is old and well known. In the instant case there is no patentable distinction between the compositional claims and claims 14, 15, and 25 which recite the term "kit." However, Lopresti et al. do not teach a composition comprising T3S and thyroxine.

Herfindal et al. teach thyroid preparations containing T3 and T4 and dosing guidelines for treating patients with hypothyroidism. (Herfindal et al. In: Clinical Pharmacy and Therapeutics. 1992, pages 289-291; see especially page 291, Table 16.9).

Mol et al. teach methods for synthesizing sulfate derivatives of iodothyronines (Mol et al. Synthesis and some properties of sulfate esters and sulfamates of iodothyronines. Endocrinology. 1985; 117(1):1-7, abstract only). Mol et al. also teach that the availability of large quantities pf [ure iodothronine sulfates and sulfamates should facilitate the study of the importance of sulfate conjugation in the metabolism of thyroid hormone.

Based on the teaching of Mol et al., someone of skill in the art would have been motivated to combine the above cited prior art references to create the instant claimed inventive concept.

Thus, someone of skill in the art at the time the instant invention was made would have found it obvious to create the instant claimed invention with reasonable predictability.

Applicant's attention is further drawn to MPEP at §2144.05, which states, "[t]he normal desire of scientists or artisans to improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage range is the optimum combination of percentages... Where the general condition of a claim are disclosed in the prior, it is not inventive to discover the optimum or workable ranges by routine experimentation."

Relevant Art of Record

The below art reference made of record and relied upon is considered pertinent to applicant's invention.

Mol et al. teach methods for synthesizing sulfate derivatives of iodothyronines (Mol et al. Synthesis and some properties of sulfate esters and sulfamates of iodothyronines. Endocrinology. 1985; 117(1):1-7, abstract only). Mol et al. also teach that the availability of large quantities pf [ure iodothronine sulfates and sulfamates should facilitate the study of the importance of sulfate conjugation in the metabolism of thyroid hormone.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charlesworth Rae whose telephone number is 571-272-6029. The examiner can normally be reached between 9 a.m. to 5:30 p.m. Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached at 571-272-0718. The

fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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25 October 2007
CER

BRIAN-YONG S. KWON
PRIMARY EXAMINER